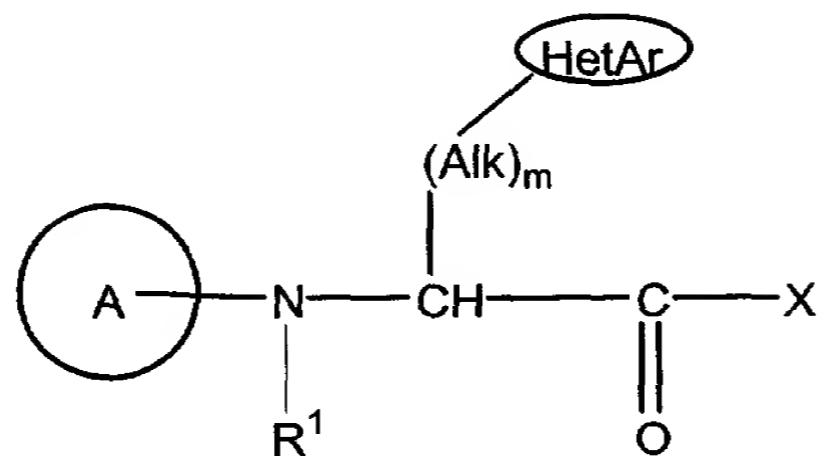


WHAT IS CLAIMED IS:

1. A compound of Formula (I):



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(I)

wherein:

A is an aryl, heteroaryl, cycloalkyl, or heterocyclic group wherein said aryl, heteroaryl, cycloalkyl, or heterocyclic group is optionally substituted, on any ring atom capable of substitution, with 1-3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, acyl, acylamino, thiocabonylamino, acyloxy, amino, substituted amino, amidino, alkyl amidino, thioamidino, aminoacyl, aminocabonylamino, aminothiocabonylamino, aminocabonyloxy, aryl, substituted aryl, aryloxy, substituted aryloxy, aryloxyaryl, substituted aryloxyaryl, cyano, halogen, hydroxyl, nitro, oxo, carboxyl, cycloalkyl, substituted cycloalkyl, guanidino, guanidinosulfone, thiol, thioalkyl, substituted thioalkyl, thioaryl, substituted thioaryl, thiocycloalkyl, substituted thiocycloalkyl, thioheteroaryl, substituted thioheteroaryl, thioheterocyclic, substituted thioheterocyclic, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, cycloalkoxy, substituted cycloalkoxy, heteroaryloxy, substituted heteroaryloxy, heterocyclxyloxy, substituted heterocyclxyloxy, oxycarbonylamino, oxythiocarbonylamino, -OS(O)₂-alkyl, -OS(O)₂-substituted alkyl, -OS(O)₂-aryl, -OS(O)₂-substituted aryl, -OS(O)₂-heteroaryl,

-OS(O)₂-substituted heteroaryl, -OS(O)₂-heterocyclic, -OS(O)₂-substituted heterocyclic, -OSO₂-NRR where each R is independently hydrogen or alkyl, -NRS(O)₂-alkyl, -NRS(O)₂-substituted alkyl, -NRS(O)₂-aryl, -NRS(O)₂-substituted aryl, -NRS(O)₂-heteroaryl, -NRS(O)₂-substituted heteroaryl, -NRS(O)₂-heterocyclic, -NRS(O)₂-substituted heterocyclic, -NRS(O)₂-NR-alkyl, -NRS(O)₂-NR-substituted alkyl, -NRS(O)₂-NR-aryl, -NRS(O)₂-NR-substituted aryl, -NRS(O)₂-NR-heteroaryl, -NRS(O)₂-NR-substituted heteroaryl, -NRS(O)₂-NR-heterocyclic, -NRS(O)₂-NR-substituted heterocyclic where R is hydrogen or alkyl, -N[S(O)₂-R']₂ and -N[S(O)₂-NR']₂ where 5 each R' is independently selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

HetAr is a nitrogen containing heteroaryl or a nitrogen containing substituted heteroaryl group;

15 Alk is an alkylene group of 1 to 4 carbons;

m is 0 or 1;

20 R¹ is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

X is selected from the group consisting of hydroxyl, alkoxy, substituted alkoxy, alkenoxy, substituted alkenoxy, cycloalkoxy, substituted cycloalkoxy, cycloalkenoxy, substituted cycloalkenoxy, aryloxy, substituted aryloxy, heteroaryloxy, substituted heteroaryloxy, heterocyclyloxy, 25 substituted heterocyclyloxy and -NR"R" where each R" is independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

and enantiomers, diasteromers and pharmaceutically acceptable salts thereof;

and further wherein the compound of Formula (I) has a binding affinity to VLA-4 as expressed by an IC₅₀ of about 15μM or less.

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2. The compound of Claim 1 wherein HetAr is a nitrogen containing substituted heteroaryl group.

3. The compound of Claim 1 wherein HetAr is a nitrogen containing heteroaryl group that is substituted with a substituent selected from the group consisting of acyl, acylamino, acyloxy, aminoacyl, aminocarbonylamino, aminothiocarbonylamino, aminocarbonyloxy, oxycarbonylamino, oxythiocarbonylamino, thioamidino, thiocarbonylamino, aminosulfonylamino, aminosulfonyloxy, aminosulfonyl, oxysulfonylamino 15 oxysulfonyl, aryl and substituted aryl.

4. The compound of Claim 1 wherein HetAr is a nitrogen containing heteroaryl group is substituted with a group of formula -O-Z-NR¹¹R^{11'} or -O-Z-R¹² wherein R¹¹ and R^{11'} are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, and where R¹¹ and R^{11'} are joined to form a heterocycle or a substituted heterocycle, R¹² is selected from the group consisting of heterocycle and substituted heterocycle, and Z is selected from 20 the group consisting of -C(O)- and -SO₂-.

25 5. The compound of Claim 4 wherein the nitrogen containing heteroaryl group is substituted with a group of formula -OC(O)NR¹¹R^{11'} wherein R¹¹ and R^{11'} are independently selected from the group consisting of

alkyl or R¹¹ and R^{11'} are joined to form a heterocycle or a substituted heterocycle.

6. The compound of Claim 5 wherein the nitrogen containing heteroaryl group is substituted with -OC(O)N(CH₃)₂.

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7. The compound of Claim 1 wherein HetAr is a nitrogen containing heteroaryl group is substituted with an aryl or substituted aryl group.

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8. The compound of Claim 1 wherein A is a heteroaryl group which is optionally substituted with 1 to 3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen.

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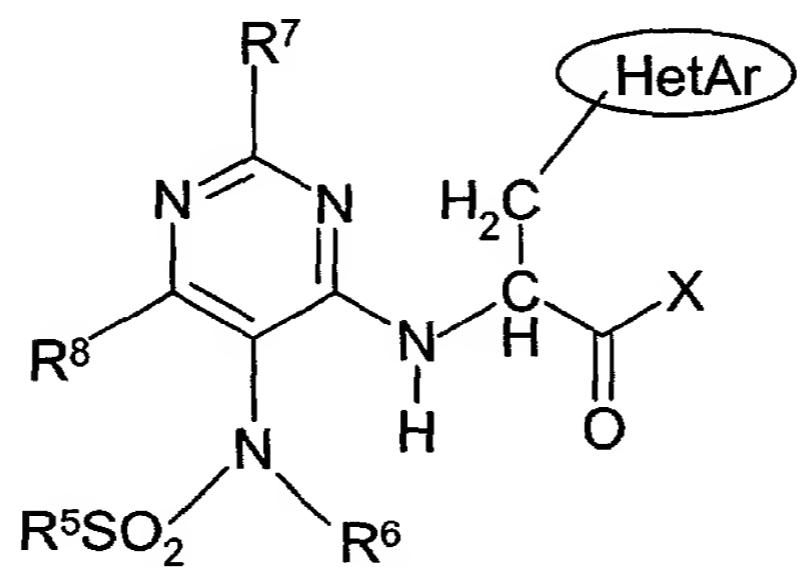
9. The compound of Claim 8 wherein A is 1-oxo-1,2,5-thiadiazole, 1,1-dioxo-1,2,5-thiadiazole, pyridazine, pyrimidine or pyrazine ring which is optionally substituted with 1 to 3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen.

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25 10. The compound of Claims 1 to 9 wherein R¹ is hydrogen, and X is hydroxyl.

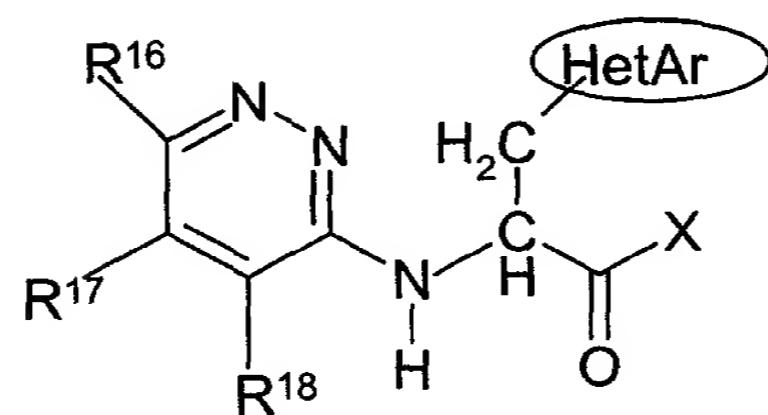
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11. The compound of Claim 1 wherein the compound has formula IIa, IIb, IIc, IId, or IIe:

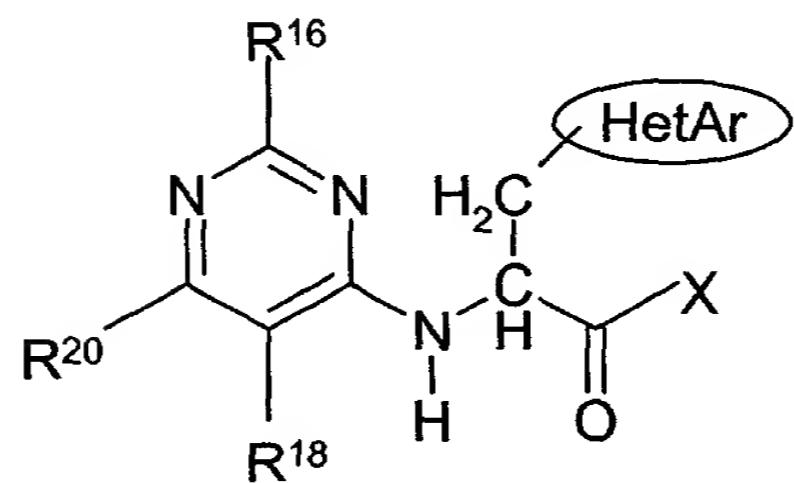


IIa

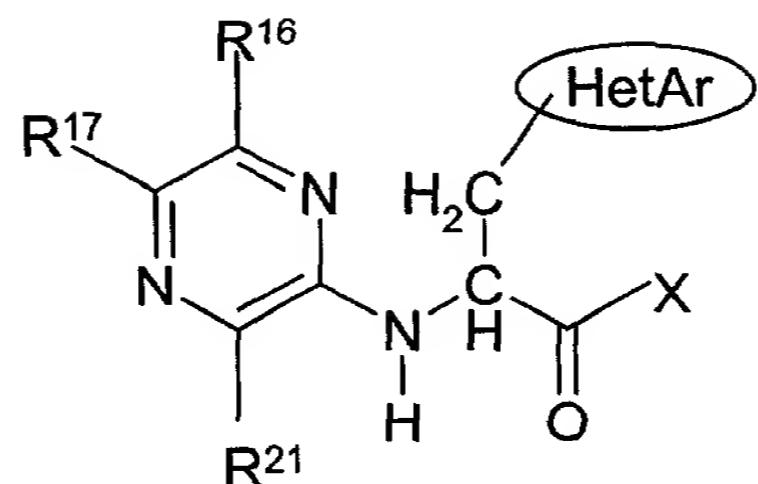
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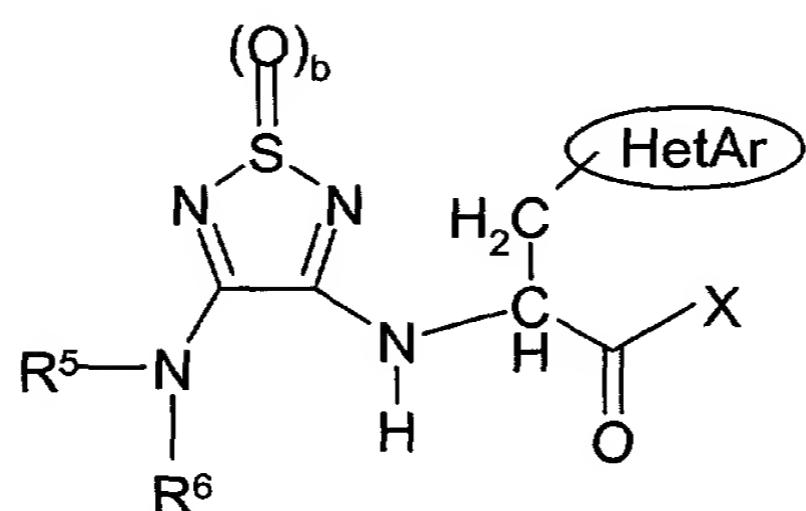
IIb



IIc



IIId,



5

IIe

wherein:

HetAr is a nitrogen containing heteroaryl group substituted with a substituent selected from the group consisting of acyl, acylamino, acyloxy, 10 aminoacyl, aminocarbonylamino, aminothiocarbonylamino, aminocarbonyloxy, oxycarbonylamino, oxythiocarbonylamino, thioamidino, thiocarbonylamino, aminosulfonylamino, aminosulfonyloxy, aminosulfonyl, oxysulfonylamino, aryl, substituted aryl, and oxysulfonyl;

R⁵ is selected from the group consisting of alkyl, substituted alkyl, 15 alkenyl, substituted alkenyl, aryl, substituted aryl, cycloalkyl, substituted

cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, heteroaryl and substituted heteroaryl;

R⁶ is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and -SO₂R¹⁰ where R¹⁰ is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl;

R⁷ and R⁸ are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

R¹⁶ and R¹⁷ are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen; and

R¹⁸ is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

R²⁰ is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

R²¹ is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclic and substituted heterocyclic;

b is 1 or 2; and

X is hydroxyl; and
and enantiomers, diastereomers and pharmaceutically acceptable salts
thereof.

5 12. The compound of Claim 11 wherein the compound is selected
from formula IIc, IIId or IIe.

10 13. The compound of Claim 11 or 12 wherein HetAr is a nitrogen
containing heteroaryl group which is substituted with a group of formula -O-
Z-NR¹¹R^{11'} or -O-Z-R¹² wherein R¹¹ and R^{11'} are independently selected from
the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl,
substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic,
substituted heterocyclic, and where R¹¹ and R^{11'} are joined to form a
heterocycle or a substituted heterocycle, R¹² is selected from the group
consisting of heterocycle and substituted heterocycle, and Z is selected from
the group consisting of -C(O)- and -SO₂-.

15 14. The compound of Claim 13 wherein the nitrogen containing
heteroaryl group is substituted with a group of formula -OC(O)NR¹¹R^{11'}
wherein R¹¹ and R^{11'} are independently selected from the group consisting of
alkyl or R¹¹ and R^{11'} are joined to form a heterocycle or a substituted
heterocycle.

20 15. The compound of Claim 14 wherein the nitrogen containing
heteroaryl group is substituted with -OC(O)N(CH₃)₂ and is at the para
position of the heteroaryl group.

25 16. The compound of Claim 11 or 12 wherein HetAr is a nitrogen
containing heteroaryl group which is substituted with an aryl or substituted
30 aryl group.

17. A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claims 1 to 16.

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18. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claims 1-16.

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